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PLEASE REPLY TO
LONDON OFFICE

25 November 2005

European Patent Office
International Searching Authority
P.B. 5818 – Patentlaan 2
2280 HV Rijswijk (ZH)
The Netherlands

Dear Sirs

Re: International Patent Application No. PCT/GB2005/000367
Sphere Medical Ltd et al.

We refer to the written opinion annexed to the international search report dated 25 July 2005 which issued in connection with the above application. In response thereto we are filing a new claim 1 as an amendment pursuant to Article 34 PCT on new pages 25. A copy of page 25 with amendments shown using "track changes" is enclosed for the examiner's assistance. A basis for this amendment may be found at page 25, lines 5-6 and 11-12.

With regard to item III of the opinion, we note the examiner's objection and we propose deferring amendment of claims 25-27 until the national/regional phases.

Before considering the objections raised under item V of the opinion, we should like to make the following comments on the interpretation of the claims.

The approach to the interpretation of claims in Europe is summarised in the introduction to the section entitled "Interpretation of claims" in the book, Case Law of the Boards of Appeal of the EPO, 4th edition 2001. Part "4.1 General" at page 168 reads:

> "The skilled person, when considering a claim, should rule out interpretations which are illogical or which do not make technical sense. He should try, with synthetical propensity, ie building up rather than tearing down, to arrive at an interpretation of the claim which is technically sensible and takes into account the whole disclosure of the patent (Art. 69 EPC). The patent must be construed by a mind willing to understand, not a mind desirous of misunderstanding (**T 190/99**)."

We are of the view that the examiner is making an overly strict interpretation of the claims of the present application in terms of the meaning of "confinement structure". We submit that this term should be given a sensible meaning taking into account the whole disclosure of the application.

The confinement structure is present on the substrate to define a first interior space. In order to be an interior space, the confinement structure must form a boundary. This is in accordance with the dictionary definition of "confine" which reads: "1. keep or restrict within certain limits; imprison. 2 limit, boundary" (Oxford English Dictionary), extract enclosed.

The confinement structure is further defined as comprising a first limiting structure. Again, "limit" is defined as "point, line, or level beyond which something does not or may not extend or pass" (Oxford English Dictionary), extract enclosed.

We therefore submit that the meaning of "confinement structure" would be immediately apparent to the skilled person.

Furthermore, page 21, lines 9-28 of the present application describes an embodiment of the present invention as it relates to a propofol sensor. Lines 12-16 describe how the chemicals forming the molecularly imprinted polymer are dissolved in hexane (a liquid). A droplet is than deposited into the confinement structure. This necessarily implies that the confinement structure and hence the first limiting structure must form a boundary around the first limiting space.

This feature of claim 1 must therefore be given due weight when reading claim 1.

Turning to item V of the written opinion, the examiner refers to D1-D8. We shall address each in turn.

D2 (and D1)

D1 is an intermediate document. However this is somewhat academic given that the US equivalent, D2, was published before the earliest priority date of the present application.

D2 (and D1) makes no mention of the electrodes being used to confine the polymer. D2 discloses the employment of contact pads to border the polymer on two sides only. In D2, the electrodes cannot confine the fluid in all directions, as at least one non-conducting gap is required between the electrodes. As a result the "first interior space" in D2 is not in any way limited. Accordingly, any fluid introduced into the device of D2 would escape through this gap.

The manufacturing principle in D2 involves the attachment of electrodes perpendicular to the substrate in order to generate any confinement effect in one direction only. In most micromachining, printed-circuit, and screen-printed techniques, one can only (readily) manufacture planar structures, e.g. electrodes, with lateral dimensions typically larger than the height of the structure. Due to the small height of structures created using these techniques, the electrodes would not act to confine a fluid.

In contrast, the confinement structure of the present invention confines the polymer/solvent mixture. Claim 1 is therefore novel over D2 (and D1).

With regard to inventive step, the use of the electrodes to confine the fluid also limits the shape and area of the electrodes. If the electrodes of D2 were used to confine the fluid more than is

shown in the figures contained in D2 (e.g. by being more half-moon shaped), the current distribution through the device would no longer be uniform, affecting the sensor performance.

Moreover, as the polymer/solvent mixture is typically a fluid, any confinement which does not restrict the movement of the fluid in all (in-plane) directions, would lead to the fluid not being confined. The fluid would therefore spread out across the substrate and cover a wider area. Moreover, it is very difficult to control accurately the fluid distribution across the substrate in a repeatable manner, resulting in large variability between sensors during manufacture (e.g. due to variations in the polymer layer thickness).

In the present invention, one can accurately control the extent of the pool and the volume of mixture to be deposited into the pool. This approach leads to very repeatable properties (e.g. thickness) of the polymer layer and therefore also of the sensor. Another advantage of the pool structures is that sensors can be created in close proximity to each other without any danger of intermixing the functional layers. Hence, we can achieve a much higher packing density of sensors in a given surface area. The skilled person is also completely free to determine the shape and size of the electrodes to optimise the sensor performance, independent of any requirements of the fluid confinement.

In addition, the confinement structure is also important in the attachment (both mechanically, e.g. by shaping the confinement wall to give a clamping effect, and also chemically, e.g. by allowing reaction between the confinement wall with the polymer), improving the stability of the film and avoiding peeling.

These advantageous properties are not derivable from D2 without the benefit of hindsight from the present invention. The skilled person would not therefore consider fundamentally changing the approach taught in D2. The present invention as claimed is therefore inventive over D2.

D3 and D4

Similarly to D2, these documents do not disclose a confinement structure comprising a first limiting structure defining a first interior space within the meaning of claim 1 of the present application.

D5

D5 discloses a microwell plate for chemical and biological analysis. A first organic molecule is attached, for example, to the bottom of the well (at "moyens de fixation 24"). Then a second organic molecule is passed into the well, which has a binding function to the first organic molecule to obtain in each well chemical or biological probes formed by the reagent bound to the bottom of the well by the mutual coupling of the binding functions of the first and second organic compound.

However, the microwell plate does not have a transducer proximal to each well. Claim 1 is therefore novel over D5. D5 does make reference to electrodes in the bottom of the well and electrodes outside the well. However, these electrodes are present for functionalising the well by attaching the first organic molecule to the bottom of the well through electro-polymerisation. The electrode is not, therefore functioning as a transducer and is not used for detection purposes.

D5 is thus a very different approach to that of the present invention.

D6

D6 relates to a self-contained DNA biosensor. The biosensor, as exemplified in Fig. 3, is built up from a number of layers which have previously been fabricated. The upper layer, sampling stage 140, includes a number of openings numbered 145 which contain receptors which bind to an analyte. Biosensors of this type are manufactured as separate layers, as shown in Fig. 3, and then the separate layers are assembled. The layers need to be assembled with great accuracy in order to ensure that the individual components are correctly aligned. This assemble process uses mechanical force and/or adhesive to bind the layers together. The great accuracy needed, combined with the small size of the components, makes the manufacturing process difficult and costly.

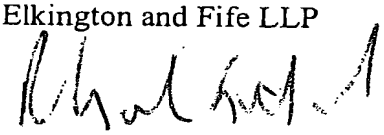
The approach used in the present invention is completely different. In the present invention, the confinement structure(s) are formed directly on the substrate by a deposition process. This deposition process is described at page 12 of the present application. The deposition is exemplified by the photo-patterning/etching and spin-coating methods, although other methods are applicable such as deposition through a patterned mask. The advantage of these processes is that the sensor forms a single unitary structure which does not require the difficult assembly of multiple layers.

Although claim 1 already states that the confinement structure is "deposited" on the substrate, claim 1 has been amended to make it more clear that the fabrication involves a deposition process. A basis for this amendment may be found at page 12, lines 5-6 and 11-12 of the international application as filed.

The deposition process of the present invention thus provides a unitary structure which is different to the structure assembled in D6 which is not unitary in nature. Claim 1 is therefore novel over D6. D6 discloses a sensor which is fundamentally different in its construction to that of the present invention and hence would not motivate the skilled person to fabricate a sensor having an integrated structure as claimed in the present application.

We submit that all of the substantive objections raised by the examiner have now been met.

Yours faithfully
Elkington and Fife LLP



Richard Gillard

Claims

1. A sensor comprising

a substrate;

a confinement structure created from materials applied to the substrate by deposition, wherein the confinement structure comprises at least a first limiting structure defining a first interior space;

a transducer proximal to the first interior space; and

a first synthetic polymer capable of selectively binding a first analyte, within the confinement structure.

2. A sensor as claimed in claim 1, wherein the confinement structure further comprises a second limiting structure defining a second interior space, the second interior space containing the first interior space.

3. A sensor as claimed in claim 2, wherein the confinement structure further comprises one or more further limiting structures defining one or more further interior spaces, the one or more further interior spaces each containing a preceding interior space.

4. A sensor as claimed in any preceding claim, wherein the first synthetic polymer capable of selectively binding a first analyte is disposed in the first interior space.

5. A sensor as claimed in any preceding claim, wherein the first synthetic polymer capable of selectively binding a first analyte is disposed in the second or one or more further interior spaces.

6. A sensor as claimed in any preceding claim, wherein the internal diameter of the first limiting structure is about 10-350 μm.

7. A sensor as claimed in any preceding claim, wherein height of the first limiting structure is about 1-10 μm.

8. A sensor as claimed in any of claims 2 to 7, wherein the internal diameter of the second limiting structure is about 50-600 μm.

Claims

1. A sensor comprising

a substrate;

a confinement structure created from materials applied to the substrate by deposition, wherein the confinement structure comprises at least a first limiting structure defining a first interior space;

a transducer proximal to the first interior space; and

a first synthetic polymer capable of selectively binding a first analyte, within the confinement structure.

Deleted: disposed on

2. A sensor as claimed in claim 1, wherein the confinement structure further comprises a second limiting structure defining a second interior space, the second interior space containing the first interior space.

3. A sensor as claimed in claim 2, wherein the confinement structure further comprises one or more further limiting structures defining one or more further interior spaces, the one or more further interior spaces each containing a preceding interior space.

4. A sensor as claimed in any preceding claim, wherein the first synthetic polymer capable of selectively binding a first analyte is disposed in the first interior space.

5. A sensor as claimed in any preceding claim, wherein the first synthetic polymer capable of selectively binding a first analyte is disposed in the second or one or more further interior spaces.

6. A sensor as claimed in any preceding claim, wherein the internal diameter of the first limiting structure is about 10-350 μm.

7. A sensor as claimed in any preceding claim, wherein height of the first limiting structure is about 1-10 μm.

8. A sensor as claimed in any of claims 2 to 7, wherein the internal diameter of the second limiting structure is about 50-600 μm.